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Long-term survival and secondary procedures after open or endovascular repair of abdominal aortic aneurysms

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ABSTRACT

Objective: Randomized trials have shown an initial survival benefit of endovascular over conventional open abdominal aortic aneurysm repair but no long-term difference up to 6 years after repair. Longer follow-up may be required to demonstrate the cumulative negative impact on survival of higher reintervention rates associated with endovascular repair.

Methods: We updated the results of the Dutch Randomized Endovascular Aneurysm Management (DREAM) trial, a multicenter, randomized controlled trial comparing open with endovascular aneurysm repair, up to 15 years of follow-up. Survival and reinterventions were analyzed on an intention-to-treat basis. Causes of death and secondary interventions were compared by use of an events per person-year analysis.

Results: There were 178 patients randomized to open and 173 to endovascular repair. Twelve years after randomization, the cumulative overall survival rates were 42.2% for open and 38.5% for endovascular repair, for a difference of 3.7 percentage points (95% confidence interval, −6.7 to 14.1; $P = .48$). The cumulative rates of freedom from reintervention were 78.9% for open repair and 62.2% for endovascular repair, for a difference of 16.7 percentage points (95% confidence interval, 5.8-27.6; $P = .01$). No differences were observed in causes of death. Cardiovascular and malignant disease account for the majority of deaths after prolonged follow-up.

Conclusions: During 12 years of follow-up, there was no survival difference between patients who underwent open or endovascular abdominal aortic aneurysm repair, despite a continuously increasing number of reinterventions in the endovascular repair group. Endograft durability and the need for continued endograft surveillance remain key issues. (J Vasc Surg 2017;66:1379-89.)

Three of the four randomized trials comparing elective open and endovascular repair of abdominal aortic aneurysms—Dutch Randomized Endovascular Aneurysm Management (DREAM), endovascular aneurysm repair (EVAR) trial 1, and Open Versus Endovascular Repair (OVER), not Anevrysme de l'aorte abdominale: Chirurgie versus Endoprothese (ACE)—have shown an early survival benefit for endovascular repair.[1-4] With longer follow-up, this advantage was absent after 1 to 2 years in the DREAM and EVAR 1 trials and after 5 years in the OVER trial.[5-7] With respect to the rate of secondary procedures, the OVER trial showed no difference between open and endovascular repair after a mean follow-up of 5.2 years.[7] The DREAM and EVAR 1 trials, however, showed a continuous decline of freedom from secondary procedures after endovascular repair, up to a median follow-up of 6.4 years and 6.0 years, respectively, whereas reinterventions after open repair occurred only sporadically after 2 to 3 years.[5,6] Secondary procedures are inevitably associated with morbidity and

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mortality; longer follow-up of the randomized trials currently available may be required to demonstrate this effect. Similarly, 5- to 6-year follow-up may be too short to identify low-incidence durability issues of endografts as well as to evaluate the cumulative effects of repeated exposure to radiation and doses of iodinated contrast agents that are a part of the obligatory endograft surveillance computed tomography (CT) scans.[8,9] Therefore, 12 years after the last patient was enrolled and 7 years after data acquisition was stopped, we updated survival and reintervention rates in participants of the DREAM trial.

ARTICLE HIGHLIGHTS

- **Type of Research:** Prospective Dutch Randomized Endovascular Aneurysm Management (DREAM) trial
- **Take Home Message:** At 12 years, the cumulative overall survival rates were 42.2% for open repair and 38.5% for endovascular aneurysm repair (EVAR) of abdominal aortic aneurysm ($P = .48$). The cumulative rates of freedom from reintervention were 78.9% for open repair and 62.2% for EVAR ($P = .01$).
- **Recommendation:** At 12 years, there was no difference in survival between open abdominal aortic aneurysm repair and EVAR, in spite of the increasing number of reinterventions after EVAR. Continued follow-up is recommended because of concerns of durability of EVAR and the need for reinterventions.

METHODS

Study design. The design and methods of the trial have been described in detail elsewhere.[10] In brief, the DREAM trial was a multicenter, randomized trial conducted at 26 centers in The Netherlands and 4 centers in Belgium. The Institutional Review Board at each center approved the original trial protocol and the follow-up extension. In the protocol, a late analysis of cumulative survival rates, secondary interventions, and causes of death was prescheduled. The study was performed according to the principles of the Declaration of Helsinki.

Study patients. Patients who had an asymptomatic abdominal aortic aneurysm measuring at least 5 cm in diameter and who were considered suitable candidates for either open or endovascular repair were enrolled after providing written informed consent. Further eligibility for inclusion in the DREAM trial and randomization procedure were described previously.[10]

The primary informed consent covered 2 years of close follow-up for all patients. For subsequent long-term analysis, a second written informed consent was obtained from all patients who had completed the initial 2 years of follow-up.[5]

Data collection. The previous data acquisition had stopped on February 1, 2009.[5] For the 229 patients reported to be alive at that moment, all relevant information from the medical records as of enrollment were reviewed at the participating centers. Data retrieved included history and physical examination at office visits, imaging reports, laboratory results, operative reports, and all available data from other specialists and hospitals. Records were scrutinized for information about survival status, causes of death, and secondary procedures. Additional information on causes and date of death was obtained by reviewing death certificates and contacting involved physicians (surgeons or general practitioners).

Patients or relatives were contacted by telephone, and with their approval and to the best of their ability, information was obtained about physical and mental health, secondary interventions, and, if applicable, date and cause of death. Cause of death and secondary intervention information were crossmatched with the data obtained from the patient's medical record and from consultation with the patient's primary care physician. Data collection ended on January 5, 2016.

For this analysis, all data were censored at the last date of contact (by telephone or follow-up). All information was integrated with data from our preceding analysis.[5]

End points. The long-term outcomes analyzed were death from all causes, aneurysm-related mortality, and secondary procedures.

Causes of death were grouped as follows: aneurysm related; cardiovascular, nonaneurysm related (myocardial infarction, cardiac arrest, congestive heart failure, stroke, and other cardiovascular); malignant disease; respiratory disease; miscellaneous; and unknown. Unknown causes of death included "natural cause" on death certificates and missing records of both trial centers and general practitioners.

Aneurysm-related mortality was defined as any death within 30 days of the initial repair or any secondary intervention, or during the hospitalization of these procedures, or any late death adjudicated as having resulted directly or indirectly from the aneurysm or its treatment.

A secondary procedure or reintervention was defined as any surgical or endovascular procedure performed after and directly or indirectly related to the primary aneurysm repair procedure. The indication for a secondary intervention was at the discretion of the individual surgeon. Secondary procedures were classified by indication into three groups: (1) aneurysm related, including incomplete aneurysm exclusions (endoleak of any type, rupture, and migration), para-anastomotic aneurysms, thrombo-occlusive events, and prosthesis infections; (2) wound related, including incisional hernia, burst abdomen (abdominal wound dehiscence in which intestine, omentum, or other viscera are visible), and wound infection; and (3) local or systemic, including bleeding, laparoscopic or laparotomic adhesiolysis or bowel resection

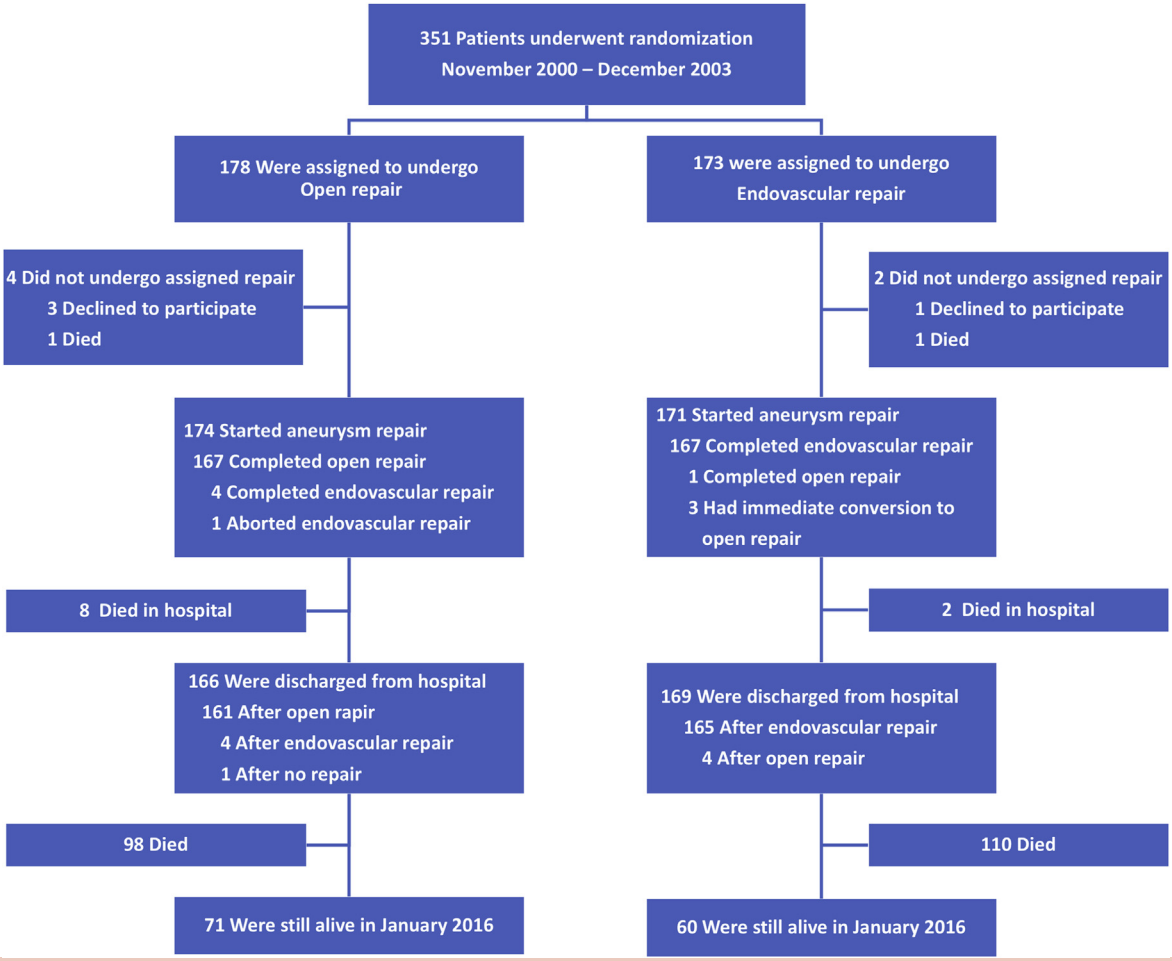

Fig 1. Consolidated Standards of Reporting Trials diagram. Randomization, distribution, and survival numbers.

for ileus, and miscellaneous, including renal artery overstenting, iatrogenic ureteral damage, and necrotizing cholecystitis.

An outcome adjudication committee, consisting of vascular surgeons, classified the causes of death and reinterventions in a blinded fashion and independently from each other. Disagreements were resolved in a plenary consensus meeting.

Data analysis. All data were analyzed according to the intention-to-treat principle. The completeness of follow-up was calculated as the ratio of the total observed person-time of follow-up to the potential time of follow-up in the study.[11] Kaplan-Meier analysis was used to calculate survival and freedom from reintervention. Differences between groups were compared with the use of the log-rank test.

To investigate a time-dependent variation in the rate of causes of death and secondary procedures, three follow-up periods were distinguished, roughly corresponding to (1) the episode of early endovascular benefit (0-6 months after randomization, including the preoperative period and hospitalization after initial aneurysm treatment), (2) the episode of overlapping survival rates in the previous midterm analysis (6 months to 6 years after randomization), and (3) the new prolonged follow-up episode between 6 and 15 years after randomization. For each episode and event, person-years at risk and events per 100 person-years per randomized group were calculated. Conditional maximum likelihood estimate rate ratios were calculated by dividing the event rate per 100 person-years after open repair by the event rate per 100 person-years after endovascular repair. Confidence intervals (CIs) and statistical differences of rate ratios were calculated using OpenEpi.com.

All reported *P* values are two sided without correction for multiple testing.

RESULTS

Patient characteristics and follow-up. Between November 2000 and December 2003, 178 patients were randomly assigned to undergo open repair and 173 to undergo endovascular repair (Fig 1). Baseline characteristics are shown in Table I. The mean age of the

Table I. Baseline characteristics of the patients

Characteristic	Open repair (n = 178)	Endovascular repair (n = 173)	*P* value
Age, years	69.6 ± 6.8	70.7 ± 6.6	.13
Male sex	161 (90)	161 (93)	.44
Mild, moderate, or severe SVS/ISCVS risk factor score[a]			
Diabetes mellitus	9.6	10.4	.86
Tobacco use	55.1	64.2	.10
Hypertension	54.5	58.4	.52
Hyperlipidemia	52.6	47.0	.33
Carotid disease	15.2	14.5	.88
Cardiac disease	46.6	41.0	.33
Renal disease	8.4	7.5	.85
Pulmonary disease	18.5	27.7	.04
Sum of SVS/ISCVS risk factor scores[a]	4.5 ± 2.5	4.4 ± 2.5	.61
FEV_1, L/s	2.6 ± 0.7	2.5 ± 0.7	.27
Body mass index, kg/m^2	26.6 ± 4.1	26.3 ± 3.4	.47
ASA class			
1 Healthy status	44 (25)	37 (22)	.53
2 Mild systemic disease	110 (62)	122 (71)	.09
3 Severe systemic disease	24 (14)	14 (8)	.12
Medication use			
β-Adrenergic blockers	92 (52)	76 (44)	.17
Statins[b]	72 (42)	63 (37)	.44
Antiplatelet agents	72 (40)	70 (41)	1.00
Angiotensin-converting enzyme inhibitors	50 (28)	58 (34)	.30
Calcium channel blockers	32 (18)	30 (17)	.89
Anticoagulants	27 (15)	20 (12)	.35

ASA, American Society of Anesthesiologists; *FEV_1*, forced expiratory volume in 1 second.
Categorical variables are presented as number (%). Continuous variables are presented as mean ± standard deviation. Because of rounding, not all percentages total 100.
[a]The Society for Vascular Surgery/International Society for Cardiovascular Surgery (SVS/ISCVS) risk factor score ranges for each of eight domains from 0 (no risk factors) to 3 (severe risk factors). Total scores can range from 0 to 24, with higher scores indicating more risk factors.
[b]No information was available for six patients in the open repair group and four patients in the endovascular repair group.

participants was 70 years, 92% were male, and 44% had concomitant cardiac disease.

In the open repair group, 166 patients were discharged from the hospital (including 1 without repair and 4 after endovascular repair); in the endovascular repair group, 169 patients were discharged from the hospital (including 4 after open repair; Fig 1). The median follow-up was 10.2 years (quartile range, 5.0-12.5 years). The completeness of follow-up was 98.4% (37.177/37.775 months) for all patients, 98.9% (19.054/19.267 months) for open repair, and 97.9.% (18.123/18.507 months) for endovascular repair. Eight patients were lost to follow-up, three (1.7%) after open and five (2.9%) after endovascular repair.

Long-term aneurysm surveillance after the 2 years of close follow-up prescribed by the DREAM trial protocol varied by institution. Nevertheless, most surviving patients were still actively scheduled for return visits 5 years after inclusion in the trial. The median duration of local outpatient surveillance was 5.1 years after open repair compared with 5.8 years after endovascular repair. At 5 years, 77.5% of surviving patients in the open repair group had visited their vascular surgeon compared with 90.0% in the endovascular repair group. At this time point, only about one-fourth of patients in the open repair group had had abdominal CT angiography compared with almost all patients in the endovascular repair group. After 10 years, 22.5% of surviving patients in the open repair group and 68.3% in the endovascular repair group remained under active surveillance. These rates had dropped to 11.3% and 50% by 12 years, respectively.

Survival. Twelve years after randomization, the cumulative overall survival rates were 42.2% for open repair and 38.5% for endovascular repair, for a difference of 3.7 percentage point (95% CI, −6.7 to 14.1; $P = .48$; Fig 2, *A*). Of all patients, 50.2% were still alive 10 years after inclusion in the trial.

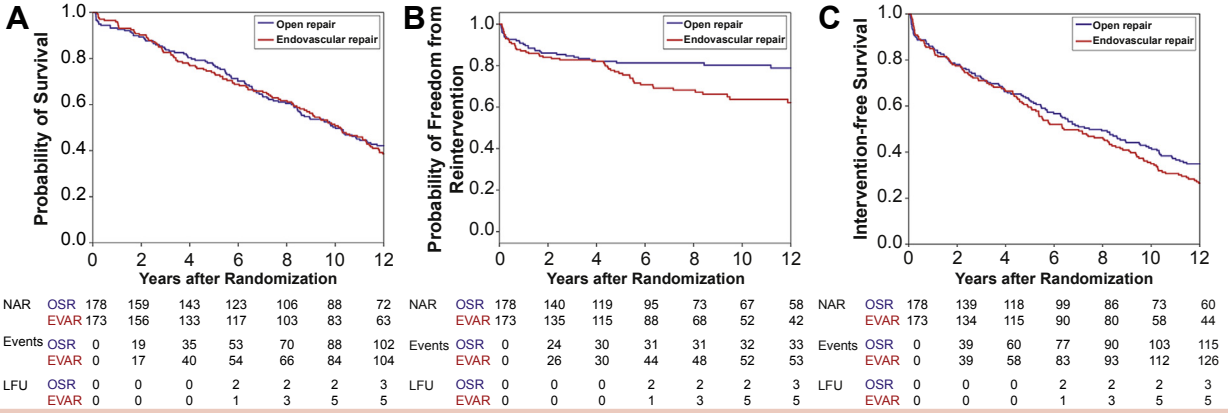

Fig 2. **A,** Kaplan-Meier estimates of survival among patients assigned to undergo open surgical repair (*OSR*) or endovascular aneurysm repair (*EVAR*). **B,** Kaplan-Meier estimates of freedom from reintervention among patients assigned to undergo OSR or EVAR. **C,** Kaplan-Meier estimates of intervention-free survival among patients assigned to undergo OSR or EVAR. *LFU,* Lost to follow-up; *NAR,* number at risk.

We were unable to crossmatch the causes of 12 of 220 (5%) deaths. In four cases, the cause of death communicated by family members could not be verified because of documentation or general practitioners being unavailable or patients having moved abroad. In eight cases, no information about cause of death was obtained from general practitioners or family members.

No differences were observed in aneurysm-related mortality between groups 12 years after randomization: 7.7% after open repair and 3.1% after endovascular repair, for a difference of 4.6 percentage points (95% CI, −9.6 to 0.4; $P = .33$). In the first 6 months, deaths were predominantly classified as aneurysm related (Table II). In contrast to the initial advantage for endovascular repair in terms of aneurysm-related mortality, no significant differences were found in all-cause mortality, aneurysm-related mortality, or mortality due to cardiovascular or malignant disease in the long term.

Beyond 6 years of follow-up, more patients died of pulmonary diseases in the open repair group (11 patients or 1.7 events per 100 person-years) compared with the endovascular repair group (2 patients or 0.3 event per 100 person-years), for an event rate ratio of 6.0 (95% CI, 1.49-39.9; $P < .01$; Table II).

There were four deaths from aneurysm rupture, two in each randomization group. One of the ruptures occurred before surgery in a patient randomized to open repair and another in a patient who had crossed over to endovascular repair, so all three postoperative deaths from aneurysm rupture occurred after endovascular repair. Besides these fatal aneurysm ruptures, one additional patient in the endovascular repair group survived ruptured aneurysm repair.

Secondary procedures. Twelve years after randomization, the cumulative rates of freedom from secondary procedure were 78.9% for open repair and 62.2% for endovascular repair, for a difference of 16.7 percentage points (95% CI, 5.8-27.6; $P = .01$; Fig 2, *B*).

Reintervention-free survival was 34.9% for open repair and 26.5% for endovascular repair 12 years after randomization, for a difference of 8.4 percentage points (95% CI, −1.3 to 18.11; $P = .13$; Fig 2, *C*).

The accumulation of all secondary procedures, including multiple reinterventions per patient, is depicted in Fig 3. In total, 143 secondary procedures were performed in 87 patients, 44 secondary procedures in 33 patients in the open repair group (2.8 events per 100 person-years) and 99 secondary procedures in 54 patients in the endovascular repair group (6.6 events per 100 person-years), for an event rate ratio of 0.42 (95% CI, 0.30-0.60; $P < .001$; Table III). This difference was predominantly determined by aneurysm-related indications, specifically reinterventions for incomplete aneurysm exclusion (event rate ratio of 0.04; 95% CI, 0.01-0.14; $P < .001$) and thrombo-occlusive indications (event rate ratio of 0.28; 95% CI, 0.10-0.68; $P < .01$; Table III).

Although secondary procedures in the endovascular repair group continued to be performed throughout the entire follow-up, the event rate per 100 person-years dropped from 24.7 (95% CI, 15.3-37.7) in the first 6 months to 6.4 (95% CI, 4.8-8.5) in the midterm and 3.7 (95% CI, 2.5-5.5) in the subsequent long-term episode.

An increased intervention rate is observed after 4 years of follow-up (Fig 2, *B*). This period was characterized by secondary interventions related to endograft durability. In this period, 12 procedures were performed because of an incomplete aneurysm exclusion and 4 for thrombo-occlusive disease. Of these interventions, one was performed in a patient with a ruptured aneurysm and one with a symptomatic aneurysm.

Conversion from endovascular to open repair occurred in 19 patients (1.2 events per 100 person-years; 95% CI, 0.7-1.8), with an event rate dropping from 5.9 (95% CI, 2.2-13.0) in the first 6 months to 0.3 (95% CI, 0.1-0.9) beyond 10 years.

Table II. Causes of death after open repair and endovascular aneurysm repair (*EVAR*)

Cause of death No. entering period No. lost to follow-up	0-6 months				>6 months-6 years	
	Open repair (n = 178)	EVAR (n = 173)	RR[a] (95% CI)	*P* value	Open repair (n = 168)	EVAR (n = 167)
Event incidence (incidence rate/100 person-years)						
Any cause	10 (11.7)	6 (7.1)	1.65 (0.60-4.90)	.34	43 (5.1)	48 (6.1)
Aneurysm related	10 (11.7)	3 (3.5)	3.31 (0.96-14.93)	.06	2 (0.2)	2 (0.3)
Rupture	1[d]	0	Undefined	.50	1[i]	0
Infection prosthesis	2	0	Undefined	.25	0	2
Other, <30 days of procedure[c]	7[e]	3[f]	2.31 (0.61-11.01)	.23	1[j]	0
Cardiovascular, not aneurysm related	0 (0)	1 (1.2)	0 (0.0-18.84)	.50	14 (1.6)	12 (1.5)
Myocardial infarction	0	0	0	0	4	2
Cardiac arrest	0	0	0	0	2	3
Congestive heart failure	0	0	0	0	4	5
Stroke	0	0	0	0	4	2
Other cardiovascular	0	1[g]	0 (0.08-18.84)	.50	0	0
Malignant disease	0 (0)	1 (1.2)	0 (0.08-18.84)	.50	15 (1.7)	16 (2.0)
Pulmonary disease	0 (0)	1[h] (1.2)	0 (0.08-18.84)	.50	3 (0.4)	5 (0.6)
Miscellaneous	0 (0)	0 (0)	0	0	3[k] (0.4)	7[l] (0.8)
Unknown	0 (0)	0 (0)	0	0	6 (7.1)	6 (7.6)

CI, Confidence interval; *RR*, rate ratio.
[a]Conditional maximum likelihood estimate rate ratio: the ratio between the overall event incidence rate per 100 person-years after open repair divided by the overall event incidence rate per 100 person-years after endovascular repair.
[b]Rate ratio: $P < .05$.
[c]Within 30 days of the initial repair or any secondary intervention, or during the hospitalization of these procedures.
[d]The cause of death was a ruptured abdominal aortic aneurysm before scheduled repair.
[e]The causes of death were as follows: anastomotic bleeding, myocardial infarction, cardiac arrest, ischemic bowel, intraoperative anaphylactic shock, multiorgan failure after repair of a burst abdomen, and progressive dementia.
[f]The causes of death were as follows: myocardial infarction, bilateral pneumonia, and one not documented.
[g]The cause of death was a pulmonary embolism, 3 months after discharge.
[h]This patient died 84 days after randomization, before undergoing aneurysm repair, from pneumonia with pre-existent pulmonary fibrosis.
[i]The cause of death was a ruptured abdominal aortic aneurysm in a patient who had crossed over to endovascular repair.
[j]The cause of death was a cardiac arrest 2 days after intervention.
[k]The causes of death were gastrointestinal bleeding, sepsis after acute pancreatitis and cholangitis, and uremia after severe dehydration.
[l]The causes of death were as follows: twice from a gastrointestinal bleeding, complications of diaphragmatic hernia repair, suicide, liver failure associated with alcohol abuse, complications of hip fracture surgery, and dehydration from obstructive bowel disease.
[m]The cause of death was systemic inflammatory response syndrome from *Enterobacter* pneumosepsis.
[n]The causes of death were twice from dementia, a subdural hematoma, and cachexia.
[o]The cause of death was dehydration from obstructive bowel disease.
[p]The causes of death were as follows: ischemia of the lower leg and refusal of further treatment and a ruptured thoracic aneurysm.
[q]The causes of death were as follows: three from dementia, subdural hematoma, major neurotrauma, urosepsis, and acute renal failure on dehydration from diabetic foot.

Of all secondary procedures, 89 (62.2%) were open surgical, 45 (31.5%) were endovascular procedures, 8 were a hybrid of open and endovascular procedures, and 1 reintervention was performed laparoscopically.

DISCUSSION

The principal finding after 12 to 15 years of follow-up of this randomized study is that in patients with infrarenal abdominal aortic aneurysms, there is no significant difference in overall survival between open and endovascular repair, despite a continuously increasing number of secondary procedures after endovascular repair.

This study reconfirms that there is only an early survival benefit for endovascular repair as shown previously by the DREAM trial and two of the three other randomized trials comparing elective open and endovascular repair of abdominal aortic aneurysm (EVAR 1 and OVER, not ACE).[1-4] Until recently, the reported median follow-up of these trials was between 5.2 and 6.4 years.

We hypothesized that longer follow-up of the randomized trials would be required to demonstrate the cumulative negative impact on overall survival from secondary procedures after endovascular abdominal aortic aneurysm repair. This study could not demonstrate such an effect. The impact of the continuously increasing number of reinterventions, the durability issues of endovascular grafts, and the cumulative irradiation effects of the increased use of CT for endograft surveillance did not accumulate to a significant survival disadvantage after endovascular repair.

Table II. Continued.

6-15 years				Total					
RR (95% CI)	*P* value	Open repair (n = 125) (n = 2)	EVAR (n = 119) (n = 1)	RR (95% CI)	*P* value	Open repair (n = 175) (n = 3)	EVAR (n = 168) (n = 5)	RR (95% CI)	*P* value[b]
Event incidence (incidence rate/100 person-years)									
0.83 (0.55-1.26)	.38	54 (8.3)	59 (8.3)	1.0 (0.69-1.45)	1.0	107 (6.7)	113 (7.5)	0.90 (0.69-1.17)	.41
0.93 (0.10-8.92)	.95	1 (0.2)	3 (0.4)	0.36 (0.01-3.41)	.42	13 (0.8)	8 (0.5)	1.54 (0.64-3.90)	.35
Undefined	.52	0	2	0.0 (0.0-3.79)	.27	2	2	0.95 (0.09-9.09)	.96
0.0 (0.0-3.23)	.23	0	0	0.0	0	2	2	0.95 (0.09-9.09)	.96
Undefined	.52	1[m]	1[o]	1.09 (0.03-42.61)	.96	9	4	2.13 (0.67-7.95)	.21
1.08 (0.50-2.40)	.84	14 (2.1)	11 (1.5)	1.39 (0.63-3.15)	.42	28 (1.8)	24 (1.6)	1.10 (0.64-1.92)	.73
1.86 (0.33-14.51)	.51	3	3	1.09 (0.19-6.36)	.92	7	5	1.32 (0.41-4.56)	.65
0.62 (0.07-4.17)	.63	2	1	2.19 (0.17-64.45)	.58	4	4	0.95 (0.21-4.19)	.94
0.74 (0.18-2.93)	.67	6	2	3.28 (0.69-23.59)	.14	10	7	1.35 (0.51-3.76)	.55
1.86 (0.33-14.51)	.51	3	3	1.09 (0.19-6.36)	.92	7	5	1.32 (0.41-4.56)	.65
0.0	0	0	2[p]	0.0 (0.0-3.79)	.27	0	3	0.00 (0.00-1.62)	.11
0.87 (0.42-1.78)	.70	14 (2.1)	19 (2.7)	0.81 (0.39-1.61)	.54	29 (1.8)	36 (2.4)	0.76 (0.46-1.24)	.28
0.56 (0.11-2.41)	.45	11 (1.7)	2 (0.3)	6.01 (1.49-39.91)	<.01	14 (0.9)	8 (0.5)	1.66 (0.70-4.16)	.26
0.40 (0.08-1.52)	.19	4[n] (0.6)	7[q] (1.0)	0.62 (0.16-2.16)	.47	7 (0.4)	14 (0.9)	0.47 (0.18-1.16)	.10
0.93 (0.28-3.05)	.90	10 (1.5)	17 (2.4)	0.64 (0.28-1.40)	.27	16 (1.0)	23 (1.5)	0.66 (0.34-1.25)	.20

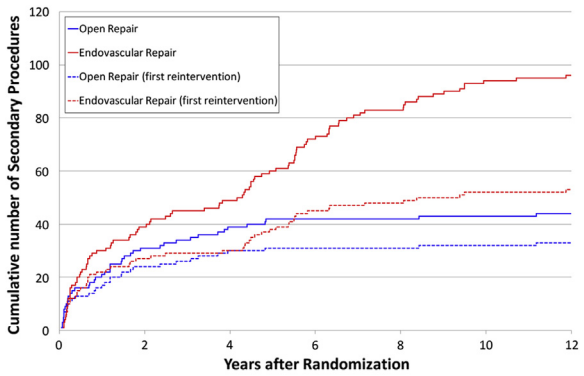

Fig 3. Cumulative number of secondary procedures over time. The *solid lines* reflect all reinterventions and the *dashed lines* only the first reintervention in a patient.

However, in a recent report of the EVAR 1 study group, increased mortality after endovascular repair was demonstrated beyond 8 years following randomization.[12] This effect was caused by a higher risk of rupture and aneurysm-related mortality. In addition, malignant disease was seen more frequently as a cause of death after endovascular repair. This phenomenon might potentially be explained by ionizing radiation during aggressive surveillance of endografts. Regarding this hypothesis, we did find a nonsignificant larger number of cancer deaths in the endovascular repair group, particularly in the long term; our data, however, did not provide further evidence to that of the EVAR 1 trial for an association between long-term cancer deaths after endovascular repair and an increased dose of CT-related radiation.[8,9,12]

When analyzing causes of death in specific follow-up time frames, we demonstrated a time-dependent variation. After the known initial survival benefit of endovascular repair in the first 6 months and the subsequent disappearance of this advantage in the midterm between 6 months and 6 years, a further parallel course of the survival curves beyond 6 years is noticed.

Despite the fact that we did not observe an increased aneurysm-related mortality, the occurrence of death due to aneurysm rupture beyond 6 years of follow-up in two patients after endovascular repair illustrates the lack of durability and emphasizes the need for continued close surveillance of endografts. This problem is reinforced by the number of stent-related secondary interventions after endovascular repair in the period beyond 6 years after randomization.

Although we have shown durability issues of endografts over the entire follow-up period and a persistent increased risk of secondary intervention, this does not amount to a significant overall survival disadvantage after endovascular repair.

Table III. Indications for secondary procedure after open repair and endovascular aneurysm repair (*EVAR*)

Indication for reintervention No. entering period No. lost to follow-up	0-6 months				>6 months-6 years	
	Open repair (n = 178)	EVAR (n = 173)	RR[a] (95% CI)	*P* value	Open repair (n = 168)	EVAR (n = 167)
Event incidence (incidence rate/100 person-years)						
Any indication	16 (18.6)	21 (24.7)	0.76 (0.39-1.45)	.40	26 (3.1)	51 (6.5)
Aneurysm-related indication	2 (2.3)	14 (16.5)	0.14 (0.02-0.55)	.002	9 (1.1)	38 (4.8)
Incomplete exclusion	0	10	0.0 (0.0-0.35)	<.001	3	22
Para-anastomotic aneurysm	0	0	0.0	0	2	0
Prosthesis infection	0	0	0.0	.50	0	3
Thrombo-occlusive	2	4	0.50 (0.06-2.80)	.44	4	13
Wound-related indication	4 (4.7)	2 (2.4)	1.98 (0.35-15.48)	.46	16 (1.9)	9 (1.1)
Wound complications	1	2	0.50 (0.02-6.52)	.62	0	4[f]
Incisional hernia	3	0	Undefined	.13	16	5
Local or systemic indication	10 (11.7)	5 (5.9)	1.98 (0.68-6.42)	.22	1 (0.1)	4 (0.5)
Bleeding	6	3	1.98 (0.49-9.71)	.35	1	1
Bowel resection or ileus	4[c]	1[d]	3.97 (0.50-98.15)	.22	0	1[g]
Miscellaneous	0	1[e]	0.0 (0.0-18.84)	.50	0	2[h]

CI, Confidence interval; *RR*, rate ratio.
[a]Conditional maximum likelihood estimate rate ratio: the ratio between the overall event incidence rate per 100 person-years after open repair divided by the overall event incidence rate per 100 person-years after endovascular repair.
[b]Rate ratio: $P < .05$.
[c]The indications for secondary intervention were adhesiolysis because of bowel obstruction, a small bowel resection because of obstruction, a laparotomy under suspicion of colonic ischemia, and a second repeated laparotomy after severe postoperative hemorrhage.
[d]The reintervention was a repeated laparotomy for unexplained gastrointestinal pain.
[e]The indication for reintervention was an infected femoral-femoral crossover.
[f]The indications for reintervention were as follows: groin wound revision with scar excision in one, drainage of groin wound infection in one, and two procedures in one patient for infection: drainage of an intra-abdominal abscess, later followed by a one-sided excision of a stent graft limb.
[g]The reintervention was a laparoscopic biopsy because of retroperitoneal fibrosis.
[h]The indications for secondary intervention were a left-sided nephrectomy after ureter damage, caused by a laparoscopic retroperitoneal biopsy for fibrosis, and a delayed crossover to open repair after a failed endovascular attempt due to severe iliac stenosis.
[i]The reintervention was adhesiolysis for bowel obstruction.
[j]The reintervention was a Hartmann procedure after aorta-sigmoidal fistula secondary to conversion.
[k]The reinterventions were renal artery bypass after proximal stent graft extension and overstenting of the renal artery due to stent graft migration, secondary to Q fever aortitis in one, and cholecystectomy after necrotizing cholecystitis, secondary to conversion to open repair.

More than 50% of our patients are still alive, 10 years after inclusion in the trial, considering they all have at least one manifestation of cardiovascular disease (abdominal aortic aneurysm) and 44% had concomitant cardiac disease. Furthermore, cardiovascular risk management at the time of randomization was far from optimal. For example, only 40% of patients had statins prescribed at the time of randomization. A recent review of literature proves an increased cumulative long-term survival after open and endovascular repair from adequate cardiovascular risk management.[13] Nonetheless, a population-based Medicare study describing survival after open and endovascular repair in the same time frame as the DREAM trial showed overall survival rates after 8 years in the range of 45%, whereas it is roughly 60% in the DREAM trial cohort.[14,15] Although a propensity score matching was performed in this Medicare study, the fact that all patients in the DREAM trial were suitable for both open and endovascular repair may be responsible for a better initial surgical risk and therefore better long-term overall survival.

We also reconfirm that secondary procedures after endovascular repair continue to be an issue, whereas reinterventions after open repair are unusual, even with follow-up extending up to 15 years after randomization. The OVER trial showed no difference in reinterventions between open and endovascular repair after a mean follow-up of 5.2 years,[7] whereas the EVAR 1 trial also showed a continuous decline of freedom from secondary procedures after endovascular repair after a median follow-up of 12.7 years, with reinterventions after open repair occurring only sporadically after 2 to 3 years. However, the relative difference in secondary intervention rate was preeminent between hospital discharge and 4 years after randomization.[12]

The combination of three new findings in this study is a cause for concern. Not only do patients survive longer than expected after aneurysm repair, with at least half

Table III. Continued.

		>6-15 years				Total			
RR (95% CI)	*P* value	Open repair (n = 125) (n = 2)	EVAR (n = 119) (n = 1)	RR (95% CI)	*P* value	Open repair (n = 175) (n = 3)	EVAR (n = 168) (n = 5)	RR (95% CI)	*P* value[b]
Event incidence (incidence rate/100 person-years)									
0.47 (0.29-0.76)	.002	2 (0.3)	27 (3.7)	0.08 (0.01-0.29)	<.001	44 (2.8)	99 (6.6)	0.42 (0.29-0.60)	<.001
0.22 (0.10-0.44)	<.001	1 (0.2)	22 (3.1)	0.05 (0.0-0.27)	<.001	12 (0.8)	74 (4.9)	0.15 (0.08-0.27)	<.001
0.13 (0.03-0.38)	<.001	0	14	0.0 (0.0-0.26)	<.001	2	46	0.04 (0.01-0.14)	<.001
Undefined	.27	1	2	0.55 (0.02-7.18)	.68	4	2	1.89 (0.34-14.77)	.49
0.0 (0.0-1.59)	.11	0	3	0.0 (0.0-1.87)	.14	0	6	0.0 (0.0-0.61)	.01
0.29 (0.08-0.84)	.02	0	3	0.0 (0.0-1.87)	.14	6	20	0.28 (0.10-0.68)	.004
1.65 (0.73-3.91)	.23	0 (0.0)	0 (0.0)	0.0	0	20 (1.3)	11 (0.7)	1.72 (0.83-3.72)	.15
0.0 (0.0-1.04)	.05	0	0	0.0	0	1	6	0.16 (0.01-1.07)	.06
2.97 (1.13-9.08)	.03	0	0	0.0	0	19	5	3.60 (1.40-10.79)	.006
0.23 (0.01-1.85)	.19	1 (0.2)	5 (7.0)	0.22 (0.01-1.58)	.15	12 (0.8)	14 (0.9)	0.81 (0.37-1.77)	.60
0.92 (0.02-36.24)	.96	0	2	0.0 (0.0-3.79)	.27	7	6	1.10 (0.36-3.50)	.86
0.0 (0.0-17.65)	.48	1[i]	1[j]	1.09 (0.03-42.61)	.96	5	3	1.58 (0.36-8.01)	.56
0.0 (0.0-3.23)	.23	0	2[k]	0.0 (0.0-3.79)	.27	0	5	0.0 (0.0-0.78)	.03

of them living longer than 10 years after surgery, but patients in the endovascular repair group also continue to be submitted to secondary procedures, and the risk of death from aneurysm rupture is persistent over time. This observation stresses the continued need for endovascular graft surveillance, even beyond 6 years after aneurysm repair. It also calls for awareness that durability of endovascular grafts is still of utmost importance in designing new devices for endovascular repair. Lower profile and wider indications should not be achieved at the expense of higher risks for reintervention and the need for more CT follow-up.

Several limitations of this study need to be addressed. Even though the trial protocol referred to the most recent clinical practice guidelines, reintervention rates constitute a soft end point because the indication for a secondary procedure was at the discretion of the surgeon. In this respect, it is important to realize that the approach to type II endoleak after endovascular repair evolved over time. In the first decade of the DREAM trial, a rather aggressive general stance toward type II endoleak possibly led to many reinterventions that in more recent times would not have been considered appropriate.[16] On the other hand, the long-term fate of type II endoleak has not been elucidated, and currently there is still inadequate information to support a uniform approach to this problem.[17,18]

Since the initiation of this trial, endovascular devices and techniques have undergone further modification, aiming at safer and more effective aneurysm exclusion and better durability. The majority of the devices used in this trial are no longer available on the market or have been replaced by more durable systems. This limits the generalizability of the reintervention rates in this report and possibly the associated long-term survival rates.

Although we acknowledge the fact that the endografts used in this trial are outdated, we think this is an inevitable consequence of studying for long-term durability. Expanding technical possibilities allow surgeons to

choose an endovascular approach in patients with more challenging anatomy. This in combination with the use of new, lower profile devices has the potential of further compromising durability of endovascular repair.

Because four times the number of patients in the endovascular repair group remained under active outpatient surveillance compared with the open repair group, there is a risk of ascertainment bias. This may have contributed to increased discovery of graft-related complications after endovascular repair as opposed to open repair. Nevertheless, it is unlikely that clinically significant problems after open repair remain undetected for as long as 12 years. Furthermore, surveillance after the initial trial period was based on clinical practice guidelines and reflects standard clinical practice in patients who are treated for abdominal aneurysms in The Netherlands. Although differences in daily practice of endograft surveillance cannot be excluded, similar rates of follow-up were described in the long-term analysis of the EVAR 1 trial.[12]

CONCLUSIONS

In the first 6 months after randomization to either open or endovascular repair of abdominal aortic aneurysms, there is an overall survival benefit for endovascular repair. During the subsequent 12 years of follow-up, we did not find a significant difference in overall survival or aneurysm-related mortality, despite a persisting rate of secondary procedures after endovascular repair. Whereas no differences in causes of death were observed, endograft durability issues are suggested to contribute to a persistent risk of rupture and increased rate of secondary interventions up to 15 years of follow-up. This calls for continued vigilant endograft surveillance extending well into the second decade after aneurysm repair, using follow-up protocols with the least possible amount of ionizing radiation, and for a renewed awareness that endograft durability is of utmost importance in future device design.

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Writing the article: TS, KY, HV, JDB, JB
Critical revision of the article: TS, KY, HV, JDB, MS, RB, CZ, JH, JB
Final approval of the article: TS, KY, HV, JDB, MS, RB, CZ, JH, JB
Statistical analysis: TS, KY, JB
Obtained funding: JB
Overall responsibility: JB

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APPENDIX.

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